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- Published:
— with international search report
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **MATRIX METALLOPROTEINASE INHIBITORS IN COMBINATION WITH HYPOTHERMIA AND/OR RADIOTHERAPY FOR THE TREATMENT OF CANCER**

(57) Abstract: The invention provides a method of treating cancer in a subject in need of such treatment which comprises: radiotherapy, or cytotoxic therapy in combination with heat shock, and further comprises administering to the subject an effective amount of a matrix metalloproteinase.

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/02365

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K45/06 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ, WPI Data, BIOSIS, EMBASE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 07697 A (PFIZER) 26 February 1998 (1998-02-26) claims 1,8-10 page 1, line 7-17 page 20, line 7-15	1-4,6-9
X	WO 00 38717 A (SEARLE) 6 July 2000 (2000-07-06) claims 1-3,18 page 1, line 6-11 page 8, line 27-32 page 12, line 12-18	1-4,6,7, 9
X	WO 99 21583 A (WARNER-LAMBERT) 6 May 1999 (1999-05-06) claims 1,6	1,3,4
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
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- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

26 June 2003

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/02365

G.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	M.HAQ E.A.: "Addition of matrix metalloproteinase inhibition to conventional cytotoxic therapy reduces tumor implantation and prolongs survival in a murine model of human pancreatic cancer" CANCER RESEARCH, vol. 60, no. 12, 2000, pages 3207-3211, XP001042323 page 3207 page 3209	1-4,6,7
X	--- A.L.THOMAS, W.P.STEWARD: "Marimastat: the clinical development of a matrix metalloproteinase inhibitor" EXPERT OPINION ON INVESTIGATIONAL DRUGS, vol. 9, no. 12, 2000, pages 2913-2922, XP008018598 page 2913 page 2917, column 2 page 2918	1-4,6,7, 9
X	--- L.JONES E.A.: "the matrix metalloproteinases and their inhibitors in the treatment of pancreatic cancer" ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, vol. 880, 1999, pages 288-307, XP008018602 page 288 page 300	1-4,6,7, 9
X	--- YASUNOBU SAWAJI E.A.: "Transient increase of intracellular cAMP by heat shock initiates the suppression of MT1-MMP production of tumor cells" ANNALS OF THE NEW YORK ACADEMY OF SCIENCES vol. 878, 1999, pages 707-709, XP008018601 page 707 -page 708 -----	1,3,4

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 1,2,6,7-10 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.1

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

INTERNATIONAL SEARCH REPORT

International application No.
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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: —
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/02365

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Form PCT/ISA/210 (patent family annex) (July 1992)

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